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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,188	11/21/2001	Birgit Jordan	DEAV2000A051USNP	9429

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
11/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/989,188	JORDAN ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,8,9,12-19,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,8,9,12,13,16-19,49 and 50* is/are rejected.

7)☒ Claim(s) *14 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's response and amendment filed on October 13, 2008 has been entered. Claims 1, 3-5, 8, 9, 12-19, 49 and 50 are pending and under examination.

Claims Summary

2. The claims are drawn to a process for identifying a chemical compound which modulates an interaction between a human EVH1 binding domain (or a protein having said domain) and a human EVH1 domain (or a protein having said binding domain). The compound is for possible use in a medicament for treating a disorder selected from the group consisting of a cardiovascular disorder, an inflammatory disorder, and a disorder of blood vessels.

The process comprises the steps of bringing the two proteins in contact in the presence of the candidate compound, incubating the mixture with a primary and secondary labeled antibody that binds to either of the two proteins. Detection of the labeled antibody indicates that the antibody bound said EVH1 domain protein or binding domain protein. The process takes place on a solid body, such as a microtiter plate coated with the EVH1 binding domain protein. In particular embodiments, the protein having the EVH1 domain is VASP. The protein having the EVH1 binding domain is zyxin. VASP binds zyxin. Also claimed are polyclonal and

monoclonal antibodies in the incubation step of the process. In another embodiment, the antibody label is a radioactive isotope, a fluorescent dye or an enzyme, such as alkaline phosphatase, beta-galactosidase, lanthanide in a europium complex.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5, 8, 9, 12, 13, 16-20, 49 and 50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Gertler *et al.* (WO 98/01755, "Gertler"), in view of Reinhard *et al.* (*PNAS USA*, 92:7956-7960, 1995, "Reinhard") and Evangelista *et al.* (US 5,262,299, "Evangelista").

Gertler discloses a screening method for a modulator of a protein (*Mammalian Ena*, abbreviated "*Mena*") having an EVH1 binding domain that binds to EVH1 proteins such as zyxin and vinculin (abstract). In one embodiment, the modulator is a chemical compound (page 28, lines 28-32). Assays are disclosed suitable for high throughput screening assays designed to identify modulators of *Mena* or Ena-VASP-like (abbreviated *Evl*) expression and/or activity (page 23). In one embodiment, the protein is contacted with a binding partner in the presence of the candidate modulating compound. The protein and its binding pair will either complex or remain separate proteins. If a complex forms, the candidate has no modulation activity on the EVH1 protein or binding domain. If a complex does not form, then the candidate has

modulation activity on the EVH1 protein and binding protein (page 23, lines 13 through page 24, line 19). Gertler discloses that secondary antibodies may be used to detect anti-EVH1 antibodies. The assays are conducted on solid phase (page 24, lines 24-29). Also disclosed are monoclonal and polyclonal antibodies that bind to proteins comprising EVH1 domains (page 17, lines 16-30). Further, the EVH1 domain protein is a fusion protein with glutathione S-transferase (page 24, lines 24-27). Gertler suggests the use of a solid phase for the assay, however, there is no teaching about a microtiter plate as claimed by Applicant. Gertler suggests the use of labels for the antibodies, however, there is no teaching regarding the types of labels. Specifically, Gertler is silent on alkaline phosphatase or beta-galactosidase, and lanthanide in a europium complex.

However, Reinhard discloses an assay wherein a zyxin family member (p83) was coated to the surface of microtiter wells and human VASP was applied as a ligand (page 7956, column 2, first full paragraph, and page 7958, second column, first paragraph). Reinhard mentions that a human zyxin homologue was discovered (page 7959, first column, first full paragraph). Reinhard also discloses a double-label immunofluoresence assay wherein monoclonal and polyclonal antibodies labeled with rhodamine and FITC (page 7958, second column, third full paragraph, and Figure 4 caption). Further, Evangelista discloses various labels used for detection assays. The labels include lanthanide chelate (europium complex), alkaline phosphatase and beta-galactosidase (Figures 1-13).

It would have been obvious to incorporate the teachings of Reinhard and Evangelista into the method of Gertler. One would have been motivated to perform the detection assay on a solid support, such as a microtiter plate, in order to test more candidate compounds. One would have

had a reasonable expectation of success because Gertler suggests the use of a solid body, and Reinhard performs a similar assay to Applicant's assay with VASP and a zyxin family member. One would have been motivated to use the labels taught by Evangelista because Gertler suggests the use of labels for the antibodies. One would have been motivated to use Evangelista's label because Evangelista teaches that the lanthanide label is highly sensitive. As for beta-galactosidase and alkaline phosphate labels, these are common labels in the art of immunoassay, evidenced by Evangelista's Figures detailing several of the well-known labels in the art. Regarding the limitation of claim 13, wherein the monoclonal antibody is synthesized using hybridoma cells, Gertler's monoclonal antibodies anticipate this limitation. Monoclonal antibodies are only ever produced from hybridoma cells to date. Regarding the use of human VASP and zyxin in the immunoassay, one would have been motivated to use human proteins in order to discover chemical compounds appropriate for human administration should any be found effective and safe. Further, with regard to the limitations of claims 49 and 50, directed to the EVH1 domain being recombinantly produced in insect cells, this limitation is a product-by-process limitation. How the EVH1 domain is prepared is not expected to render the final product, and EVH1 domain, distinct from Gertler's protein.

With regard to the identification of the compounds resulting from steps a-d as a potential medicament for treatment of cardiovascular disorders, inflammatory disorders and disorders of the blood vessels, this step is not considered by the Office to be a limiting step. Unless Applicant is performing subsequent screening assays of the compounds, the mere step of "identifying" is not limiting. After performing steps a-d, which are the same as Gertler's method, one would arrive at the same set of compounds (modulators of EVH1). Simply saying

that the compounds are potential medicaments for treatment of cardiovascular disorders, inflammatory disorders and disorders of the blood vessels does not require any further screening (active steps). It is merely the mental step of suggesting that the compounds are potentially useful for treating those disorders.

4. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant notes that the amended claims no longer recite "use" in step e). Step e) requires the identification of the chemical compound detected as a potential medicament for treating a disorder. Applicant argues that the amendment takes step e) out of the realm of an intended use.
- In response to Applicant's argument, the Office does not consider the newly introduced limitation to be of any patentable distinction over Gertler. The modified step e) remains a mental step that is not an active step. Identifying a compound as a potential medicament does not require any active steps or protocols because it is a mental conclusion. Although the word "use" has been removed from step e), the fact remains that the compound is identified as a potential medicament, thus its potential use as a medicament. Its intended use as a medicament does not alter the method steps or reagents such that the method is distinguished over Gertler. In other words, the method steps and reagents remain the same as those described in Gertler's method. Compounds identified by Gertler's method are expected to have the same properties as those compounds identified by the instant method because the method of

identifying the compounds is the same. Applicant's modification of the claim language does not change the mental step of step e). The intended use has not changed the method such that different compounds are identified relative to Gertler's method.

- Applicant also argues that because the compounds are not being claimed, the compounds are not an issue of patentability.

- In response to Applicant's argument, the Office agrees that the compounds are not being claimed. However, the claimed method steps of Gertler are expected to result in the same compounds being identified/detected because the method steps and reagents are the same. By commenting on the compounds, the Office is reiterating that the method steps and reagents used in the method are the same as those in Applicant's method, thus the resulting compounds identified are also expected to be the same.

- Applicant argues that the identifying step e) is an active step, not merely a mental step. Applicant asserts that identifying is an activity. Applicant argues that the compounds identified in part e) and the preceding action would constitute a set of compounds that are for treatment of cardiovascular disorders, inflammatory disorders and disorders of the blood vessels.

- In response to Applicant's argument, the active steps of Applicant's method (steps a-d) are the same as those performed by Gertler. There are no distinguishing features of the steps (a-d) that would lead to a different set of compounds being identified in step e). Applicant's step of identifying a compound as a potential medicament for

treatment of cardiovascular disorders, inflammatory disorders and disorders of the blood vessels is merely "identifying", and lacks any other steps that differentiate between compounds that treat other disorders and those that treat the claimed disorders. Gertler's method results in the same compound set as Applicant's method: modulators of EVH1 activity.

- Applicant's assertion that "identifying" is an active step because it is an activity does not account for the absence of any steps that actually distinguish between the identified potential medicaments for treating the claimed disorders versus other disorders. Unless Applicant is performing subsequent screening assays of the compounds, the mere step of "identifying" is not limiting. After performing steps a-d, which are the same as Gertler's method, one would arrive at the same set of compounds (modulators of EVH1). Simply saying that the compounds are potential medicaments for treatment of cardiovascular disorders, inflammatory disorders and disorders of the blood vessels does not require any further screening (active steps). It is merely the mental step of suggesting that the compounds are potentially useful for treating those disorders.

Conclusion

5. No claim is allowed. Claims 14 and 15 are objected to for depending from rejected claims.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art

of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/
Primary Examiner, TC1600